



SEQUENCE LISTING

<110> Pepinsky, Blake
Runkel, Laura
Brickelmaier, Margot
Whitty, Adrian
Hochman, Paula

<120> Polymer Conjugates of Interferon Beta-1a
and Uses

<130> 00689-514/A065

<140> 09/832,658

<141> 2001-04-11

<150> PCT/US99/24201

<151> 1999-10-15

<150> 60/104,572

<151> 1998-10-16

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<151> 1999-02-16

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ttgaatggga ggcttgaata ctgcctcaag gacaggatga actttgacat ccctgaggag 180
attaagcagc tgcagcagtt ccagaaggag gacgccgat tgaccatcta tgagatgctc 240
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gaaaaactgg agaaagaaga tttcaccagg ggaactca tgagcagttc gcacctgaaa 420
agatattatg ggaggattct gcattacctg aaggccaagg agtacagtca ctgtgcctgg 480
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Gln	Gln	Phe	Gln	Lys	Glu	Asp	Ala	Ala	Leu	Thr	Ile	Tyr	Glu	Met	Leu
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Gln	Asn	Ile	Phe	Ala	Ile	Phe	Arg	Gln	Asp	Ser	Ser	Ser	Thr	Gly	Trp
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			100						105					110	
Asn	His	Leu	Lys	Thr	Val	Leu	Glu	Glu	Lys	Leu	Glu	Lys	Glu	Asp	Phe
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	130					135						140			
Arg	Ile	Leu	His	Tyr	Leu	Lys	Ala	Lys	Glu	Tyr	Ser	His	Cys	Ala	Trp
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<211> 76

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Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln
35 40 45
Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln
50 55 60
Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Thr Gly Trp Asn
65 70 75 80
Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn

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			100					105					110				
Arg	Gly	Ala	Leu	Met	Ser	Ser	Leu	His	Leu	Lys	Arg	Tyr	Tyr	Gly	Arg		
		115					120					125					
Ile	Leu	His	Tyr	Leu	Lys	Ala	Lys	Glu	Tyr	Ser	His	Cys	Ala	Trp	Thr		
	130					135					140						
Ile	Val	Arg	Val	Glu	Ile	Leu	Arg	Asn	Phe	Tyr	Arg	Ile	Asn	Arg	Leu		
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		20						25					30				
Lys	Asp	Arg	Met	Asn	Phe	Asp	Ile	Pro	Glu	Glu	Ile	Lys	Gln	Leu	Gln		
	35					40						45					
Gln	Phe	Gln	Lys	Glu	Asp	Ala	Ala	Leu	Thr	Ile	Tyr	Glu	Met	Leu	Gln		
	50					55					60						
Asn	Ile	Phe	Ala	Ile	Phe	Arg	Gln	Asp	Ser	Ser	Ser	Thr	Gly	Trp	Asn		
65				70					75					80			
Glu	Thr	Ile	Val	Glu	Asn	Leu	Leu	Ala	Asn	Val	Tyr	His	Gln	Ile	Asn		
			85						90					95			
His	Leu	Lys	Thr	Val	Leu	Glu	Glu	Lys	Leu	Glu	Lys	Glu	Asp	Phe	Thr		
			100					105					110				
Arg	Gly	Ala	Leu	Met	Ser	Ser	Leu	His	Leu	Lys	Arg	Tyr	Tyr	Gly	Arg		
		115					120					125					
Ile	Leu	His	Tyr	Leu	Lys	Ala	Lys	Glu	Tyr	Ser	His	Cys	Ala	Trp	Thr		
	130					135					140						
Ile	Val	Arg	Val	Glu	Ile	Leu	Arg	Asn	Phe	Tyr	Arg	Ile	Asn	Arg	Leu		
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Thr	Gly	Tyr	Leu	Arg	Asn												
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<210> 27
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<400> 27

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		20						25					30				
Lys	Asp	Arg	Met	Asn	Phe	Asp	Ile	Pro	Glu	Glu	Ile	Lys	Gln	Leu	Gln		
	35					40						45					
Gln	Phe	Gln	Lys	Glu	Asp	Ala	Ala	Leu	Thr	Ile	Tyr	Glu	Met	Leu	Gln		
	50					55					60						
Asn	Ile	Phe	Ala	Ile	Phe	Arg	Gln	Asp	Ser	Ser	Ser	Thr	Gly	Trp	Asn		
65				70					75					80			

Glu	Thr	Ile	Val	Glu	Asn	Leu	Leu	Ala	Asn	Val	Tyr	His	Gln	Ile	Asn
				85					90					95	
His	Leu	Lys	Thr	Val	Leu	Glu	Glu	Lys	Leu	Glu	Lys	Glu	Asp	Phe	Thr
			100					105					110		
Arg	Gly	Ala	Leu	Met	Ser	Ser	Leu	His	Leu	Lys	Arg	Tyr	Tyr	Gly	Arg
		115					120					125			
Ile	Leu	His	Tyr	Leu	Lys	Ala	Lys	Glu	Tyr	Ser	His	Cys	Ala	Trp	Thr
	130					135					140				
Ile	Val	Arg	Val	Glu	Ile	Leu	Arg	Asn	Phe	Tyr	Arg	Ile	Asn	Arg	Leu
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Thr	Gly	Tyr	Leu	Arg	Asn										
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<210> 28
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			20					25					30		
Ala	Asp	Arg	Met	Asn	Phe	Asp	Ile	Pro	Glu	Glu	Ile	Lys	Gln	Leu	Gln
		35				40						45			
Gln	Phe	Gln	Lys	Glu	Asp	Ala	Leu	Thr	Ile	Tyr	Glu	Met	Leu	Gln	
	50				55					60					
Asn	Ile	Phe	Ala	Ile	Phe	Arg	Gln	Asp	Ser	Ser	Ser	Thr	Gly	Trp	Asn
65				70					75					80	
Glu	Thr	Ile	Val	Glu	Asn	Leu	Leu	Ala	Asn	Val	Tyr	His	Gln	Ile	Asn
			85						90					95	
His	Leu	Lys	Thr	Val	Leu	Glu	Glu	Lys	Leu	Glu	Lys	Glu	Asp	Phe	Thr
			100					105					110		
Arg	Gly	Ala	Leu	Met	Ser	Ser	Leu	His	Leu	Lys	Arg	Tyr	Tyr	Gly	Arg
		115					120					125			
Ile	Leu	His	Tyr	Leu	Lys	Ala	Lys	Glu	Tyr	Ser	His	Cys	Ala	Trp	Thr
	130					135					140				
Ile	Val	Arg	Val	Glu	Ile	Leu	Arg	Asn	Phe	Tyr	Arg	Ile	Asn	Arg	Leu
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Thr	Gly	Tyr	Leu	Arg	Asn										
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<210> 29
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<400> 29

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			20					25					30		
Lys	Asp	Arg	Ala	Ala	Phe	Ala	Ile	Pro	Ala	Glu	Ile	Lys	Gln	Leu	Gln
		35				40						45			
Gln	Phe	Gln	Lys	Glu	Asp	Ala	Leu	Thr	Ile	Tyr	Glu	Met	Leu	Gln	
	50				55					60					
Asn	Ile	Phe	Ala	Ile	Phe	Arg	Gln	Asp	Ser	Ser	Ser	Thr	Gly	Trp	Asn

65					70					75				80	
Glu	Thr	Ile	Val	Glu	Asn	Leu	Leu	Ala	Asn	Val	Tyr	His	Gln	Ile	Asn
				85					90					95	
His	Leu	Lys	Thr	Val	Leu	Glu	Glu	Lys	Leu	Glu	Lys	Glu	Asp	Phe	Thr
			100					105						110	
Arg	Gly	Ala	Leu	Met	Ser	Ser	Leu	His	Leu	Lys	Arg	Tyr	Tyr	Gly	Arg
		115					120						125		
Ile	Leu	His	Tyr	Leu	Lys	Ala	Lys	Glu	Tyr	Ser	His	Cys	Ala	Trp	Thr
	130					135					140				
Ile	Val	Arg	Val	Glu	Ile	Leu	Arg	Asn	Phe	Tyr	Arg	Ile	Asn	Arg	Leu
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Thr	Gly	Tyr	Leu	Arg	Asn										
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			20					25					30		
Lys	Asp	Arg	Met	Asn	Phe	Asp	Ile	Pro	Glu	Glu	Ile	Ala	Ala	Ala	Ala
		35					40					45			
Ala	Phe	Ala	Ala	Ala	Asp	Ala	Ala	Leu	Thr	Ile	Tyr	Glu	Met	Leu	Gln
	50					55					60				
Asn	Ile	Phe	Ala	Ile	Phe	Arg	Gln	Asp	Ser	Ser	Ser	Thr	Gly	Trp	Asn
65				70					75					80	
Glu	Thr	Ile	Val	Glu	Asn	Leu	Leu	Ala	Asn	Val	Tyr	His	Gln	Ile	Asn
				85					90					95	
His	Leu	Lys	Thr	Val	Leu	Glu	Glu	Lys	Leu	Glu	Lys	Glu	Asp	Phe	Thr
			100					105						110	
Arg	Gly	Ala	Leu	Met	Ser	Ser	Leu	His	Leu	Lys	Arg	Tyr	Tyr	Gly	Arg
		115					120						125		
Ile	Leu	His	Tyr	Leu	Lys	Ala	Lys	Glu	Tyr	Ser	His	Cys	Ala	Trp	Thr
	130					135					140				
Ile	Val	Arg	Val	Glu	Ile	Leu	Arg	Asn	Phe	Tyr	Arg	Ile	Asn	Arg	Leu
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Thr	Gly	Tyr	Leu	Arg	Asn										
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			20					25					30		
Lys	Asp	Arg	Met	Asn	Phe	Asp	Ile	Pro	Glu	Glu	Ile	Lys	Gln	Leu	Gln
		35					40					45			
Gln	Phe	Gln	Lys	Glu	Asp	Ala	Ala	Leu	Thr	Ile	Tyr	Glu	Met	Leu	Ala
	50					55					60				

Asn	Ile	Ala	Ser	Ile	Phe	Arg	Gln	Asp	Ser	Ser	Ser	Thr	Gly	Trp	Asn
65					70					75					80
Glu	Thr	Ile	Val	Glu	Asn	Leu	Leu	Ala	Asn	Val	Tyr	His	Gln	Ile	Asn
				85					90					95	
His	Leu	Lys	Thr	Val	Leu	Glu	Glu	Lys	Leu	Glu	Lys	Glu	Asp	Phe	Thr
			100					105					110		
Arg	Gly	Ala	Leu	Met	Ser	Ser	Leu	His	Leu	Lys	Arg	Tyr	Tyr	Gly	Arg
		115					120					125			
Ile	Leu	His	Tyr	Leu	Lys	Ala	Lys	Glu	Tyr	Ser	His	Cys	Ala	Trp	Thr
	130					135					140				
Ile	Val	Arg	Val	Glu	Ile	Leu	Arg	Asn	Phe	Tyr	Arg	Ile	Asn	Arg	Leu
145				150						155					160
Thr	Gly	Tyr	Leu	Arg	Asn										
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<210> 32
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 <213> human

<400> 32

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Cys	Gln	Lys	Leu	Leu	Trp	Gln	Leu	Asn	Gly	Arg	Leu	Glu	Tyr	Cys	Leu
			20					25					30		
Lys	Asp	Arg	Met	Asn	Phe	Asp	Ile	Pro	Glu	Glu	Ile	Lys	Gln	Leu	Gln
			35				40					45			
Gln	Phe	Gln	Lys	Glu	Asp	Ala	Ala	Leu	Thr	Ile	Tyr	Glu	Met	Leu	Gln
	50					55					60				
Asn	Ile	Phe	Ala	Ile	Phe	Ala	Ala	Ala	Ser	Ser	Ser	Thr	Gly	Trp	Asn
65				70						75					80
Glu	Thr	Ile	Val	Glu	Asn	Leu	Leu	Ala	Asn	Val	Tyr	His	Gln	Ile	Asn
				85					90					95	
His	Leu	Lys	Thr	Val	Leu	Glu	Glu	Lys	Leu	Glu	Lys	Glu	Asp	Phe	Thr
			100					105					110		
Arg	Gly	Ala	Leu	Met	Ser	Ser	Leu	His	Leu	Lys	Arg	Tyr	Tyr	Gly	Arg
		115					120					125			
Ile	Leu	His	Tyr	Leu	Lys	Ala	Lys	Glu	Tyr	Ser	His	Cys	Ala	Trp	Thr
	130					135					140				
Ile	Val	Arg	Val	Glu	Ile	Leu	Arg	Asn	Phe	Tyr	Arg	Ile	Asn	Arg	Leu
145				150						155					160
Thr	Gly	Tyr	Leu	Arg	Asn										
				165											

<210> 33
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 <212> PRT
 <213> human

<400> 33

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Cys	Gln	Lys	Leu	Leu	Trp	Gln	Leu	Asn	Gly	Arg	Leu	Glu	Tyr	Cys	Leu
			20					25					30		
Lys	Asp	Arg	Met	Asn	Phe	Asp	Ile	Pro	Glu	Glu	Ile	Lys	Gln	Leu	Gln
			35				40					45			
Gln	Phe	Gln	Lys	Glu	Asp	Ala	Ala	Leu	Thr	Ile	Tyr	Glu	Met	Leu	Gln

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Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Thr Gly Trp Asn				
65	70	75	80	
Ala Ser Ile Val Ala Leu Leu Ser Asn Val Tyr His Gln Ile Asn				
	85	90	95	
His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr				
	100	105	110	
Arg Gly Ala Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg				
	115	120	125	
Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr				
	130	135	140	
Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Arg Ile Asn Arg Leu				
145	150	155	160	
Thr Gly Tyr Leu Arg Asn				
	165			

<210> 34
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 <213> human

<400> 34

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	20	25	30	
Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln				
	35	40	45	
Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln				
	50	55	60	
Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Thr Gly Trp Asn				
65	70	75	80	
Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Ala His Gln Ile Ala				
	85	90	95	
His Leu Ala Ala Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr				
	100	105	110	
Arg Gly Ala Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg				
	115	120	125	
Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr				
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Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Arg Ile Asn Arg Leu				
145	150	155	160	
Thr Gly Tyr Leu Arg Asn				
	165			

<210> 35
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 <212> PRT
 <213> human

<400> 35

Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln				
1	5	10	15	
Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu				
	20	25	30	
Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln				
	35	40	45	

Gln	Phe	Gln	Lys	Glu	Asp	Ala	Ala	Leu	Thr	Ile	Tyr	Glu	Met	Leu	Gln
50						55					60				
Asn	Ile	Phe	Ala	Ile	Phe	Arg	Gln	Asp	Ser	Ser	Ser	Thr	Gly	Trp	Asn
65					70					75					80
Glu	Thr	Ile	Val	Glu	Asn	Leu	Leu	Ala	Asn	Val	Tyr	His	Gln	Ile	Asn
				85					90					95	
His	Leu	Lys	Thr	Val	Leu	Ala	Ala	Lys	Leu	Ala	Ala	Ala	Asp	Phe	Thr
			100					105					110		
Arg	Gly	Ala	Leu	Met	Ser	Ser	Leu	His	Leu	Lys	Arg	Tyr	Tyr	Gly	Arg
		115					120					125			
Ile	Leu	His	Tyr	Leu	Lys	Ala	Lys	Glu	Tyr	Ser	His	Cys	Ala	Trp	Thr
	130					135					140				
Ile	Val	Arg	Val	Glu	Ile	Leu	Arg	Asn	Phe	Tyr	Arg	Ile	Asn	Arg	Leu
145					150					155					160
Thr	Gly	Tyr	Leu	Arg	Asn										
					165										

<210> 36
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 <212> PRT
 <213> human

<400> 36

Met	Ser	Tyr	Asn	Leu	Leu	Gly	Phe	Leu	Gln	Arg	Ser	Ser	Asn	Phe	Gln
1				5					10					15	
Cys	Gln	Lys	Leu	Leu	Trp	Gln	Leu	Asn	Gly	Arg	Leu	Glu	Tyr	Cys	Leu
		20						25					30		
Lys	Asp	Arg	Met	Asn	Phe	Asp	Ile	Pro	Glu	Glu	Ile	Lys	Gln	Leu	Gln
	35					40						45			
Gln	Phe	Gln	Lys	Glu	Asp	Ala	Ala	Leu	Thr	Ile	Tyr	Glu	Met	Leu	Gln
	50					55					60				
Asn	Ile	Phe	Ala	Ile	Phe	Arg	Gln	Asp	Ser	Ser	Ser	Thr	Gly	Trp	Asn
65					70					75					80
Glu	Thr	Ile	Val	Glu	Asn	Leu	Leu	Ala	Asn	Val	Tyr	His	Gln	Ile	Asn
				85					90					95	
His	Leu	Lys	Thr	Val	Leu	Glu	Glu	Lys	Leu	Glu	Lys	Glu	Ala	Ala	Thr
			100					105					110		
Ala	Gly	Ala	Ala	Met	Ser	Ala	Leu	His	Leu	Lys	Arg	Tyr	Tyr	Gly	Arg
		115				120						125			
Ile	Leu	His	Tyr	Leu	Lys	Ala	Lys	Glu	Tyr	Ser	His	Cys	Ala	Trp	Thr
	130					135					140				
Ile	Val	Arg	Val	Glu	Ile	Leu	Arg	Asn	Phe	Tyr	Arg	Ile	Asn	Arg	Leu
145					150					155					160
Thr	Gly	Tyr	Leu	Arg	Asn										
					165										

<210> 37
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 <212> PRT
 <213> human

<400> 37

Met	Ser	Tyr	Asn	Leu	Leu	Gly	Phe	Leu	Gln	Arg	Ser	Ser	Asn	Phe	Gln
1				5					10					15	
Cys	Gln	Lys	Leu	Leu	Trp	Gln	Leu	Asn	Gly	Arg	Leu	Glu	Tyr	Cys	Leu
			20					25					30		

Lys	Asp	Arg	Met	Asn	Phe	Asp	Ile	Pro	Glu	Glu	Ile	Lys	Gln	Leu	Gln
	35						40					45			
Gln	Phe	Gln	Lys	Glu	Asp	Ala	Ala	Leu	Thr	Ile	Tyr	Glu	Met	Leu	Gln
	50					55					60				
Asn	Ile	Phe	Ala	Ile	Phe	Arg	Gln	Asp	Ser	Ser	Ser	Thr	Gly	Trp	Asn
65					70					75					80
Glu	Thr	Ile	Val	Glu	Asn	Leu	Leu	Ala	Asn	Val	Tyr	His	Gln	Ile	Asn
				85					90					95	
His	Leu	Lys	Thr	Val	Leu	Glu	Glu	Lys	Leu	Glu	Lys	Glu	Asp	Phe	Thr
			100					105					110		
Arg	Gly	Ala	Leu	Met	Ser	Ser	Leu	His	Leu	Lys	Arg	Tyr	Tyr	Gly	Ala
	115						120					125			
Ile	Ala	Ala	Tyr	Leu	Ala	Ala	Lys	Glu	Tyr	Ser	His	Cys	Ala	Trp	Thr
	130				135						140				
Ile	Val	Arg	Val	Glu	Ile	Leu	Arg	Asn	Phe	Tyr	Arg	Ile	Asn	Arg	Leu
145					150					155					160
Thr	Gly	Tyr	Leu	Arg	Asn										
				165											

<210> 38
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 <213> human

<400> 38

Met	Ser	Tyr	Asn	Leu	Leu	Gly	Phe	Leu	Gln	Arg	Ser	Ser	Asn	Phe	Gln
1				5					10					15	
Cys	Gln	Lys	Leu	Leu	Trp	Gln	Leu	Asn	Gly	Arg	Leu	Glu	Tyr	Cys	Leu
		20						25					30		
Lys	Asp	Arg	Met	Asn	Phe	Asp	Ile	Pro	Glu	Glu	Ile	Lys	Gln	Leu	Gln
	35						40					45			
Gln	Phe	Gln	Lys	Glu	Asp	Ala	Ala	Leu	Thr	Ile	Tyr	Glu	Met	Leu	Gln
	50					55					60				
Asn	Ile	Phe	Ala	Ile	Phe	Arg	Gln	Asp	Ser	Ser	Ser	Thr	Gly	Trp	Asn
65					70					75					80
Glu	Thr	Ile	Val	Glu	Asn	Leu	Leu	Ala	Asn	Val	Tyr	His	Gln	Ile	Asn
				85					90					95	
His	Leu	Lys	Thr	Val	Leu	Glu	Glu	Lys	Leu	Glu	Lys	Glu	Asp	Phe	Thr
			100					105					110		
Arg	Gly	Ala	Leu	Met	Ser	Ser	Leu	His	Leu	Lys	Arg	Tyr	Tyr	Gly	Arg
	115						120					125			
Ile	Leu	His	Tyr	Leu	Lys	Ala	Ala	Tyr	Ser	His	Cys	Ala	Trp	Thr	
	130					135				140					
Ile	Val	Arg	Val	Glu	Ile	Leu	Arg	Asn	Phe	Tyr	Arg	Ile	Asn	Arg	Leu
145					150					155					160
Thr	Gly	Tyr	Leu	Arg	Asn										
				165											

<210> 39
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Met	Ser	Tyr	Asn	Leu	Leu	Gly	Phe	Leu	Gln	Arg	Ser	Ser	Asn	Phe	Gln
1				5					10					15	
Cys	Gln	Lys	Leu	Leu	Trp	Gln	Leu	Asn	Gly	Arg	Leu	Glu	Tyr	Cys	Leu

